Remarks

Claims 17, 19, and 21-27 are pending. Claims 17, 19 and 21-27 are rejected.

Claim Objections

Claim 21 is objected to for reciting "a lox sit[.]" Amended claim 21 no longer recites "a lox sit." The Applicants respectfully request the objection to claim 21 be removed.

35 USC § 112 Written Description Rejections

Claim 27 is rejected under 35 USC § 112 for allegedly failing to comply with the written description requirement. The rejection alleges claim 27 does not teach a representative number of species of "regulating sequence[s]." The rejection alleges that the genus of "regulating sequence[s]"in claim 27 "encompass[es] any regulating sequence, which includes enhancers, repressors, promoters, etc." and is not adequately described. The Examiner, however, correctly observes that "the specification teaches nucleic acid constructs comprising inducible and constituative promoters."

Claim 27 has been amended, consistent with the Examiner's guidance, to recite that in the claimed method "a Cre expression nucleic acid compris[es] a promoter sequence and the cre gene[.]" The Applicants note, for example, that paragraphs [0028] and [0035] in Examples 1 and 2 respectively teach the use of isolated nucleic acids comprising the *cre* gene under the control of a constituatively active promoter, and that paragraph [0010] teaches that the *cre* gene can be placed under the control of an inducible promoter or a tissue specific promoter. Consequently, the genus in claim 27 no longer is as broad as "a regulating sequence" and has been limited to "promoters" of the types described by the Specification. The Applicants respectfully request that the rejection of claim 27 under 35 USC § 112 be withdrawn.

35 U.S.C. §102(e) Anticipation Rejection

Claims 17, 19, 21-25 and 27 are rejected under 35 U.S.C. §102(e) as being anticipated by Taira. The rejection alleges that Taira teaches RNAi compounds comprising a sense sequence under the control of a promoter with an intervening first lox site, a stop transcription stop site located in between and a second lox site followed by an antisense sequence.

Independent Claim 17 has been amended to specify that the intervening DNA sequence comprises a transcription stop site and a gene encoding and antibiotic resistance marker. Taira does not teach the inclusion of an antibiotic resistance marker in the intervening DNA sequence flanked by lox sites. Consequently, Taira does not teach all of the elements in Claims 19, 21-25 and 27. Claims 17, 19-25 and 27 are thus distinguished from Taira. The Applicants respectfully request that the rejection of Claims 17, 19, 21-25 and 27 be withdrawn.

35 U.S.C. §103(a) Obviousness Rejections

Claims 17, 19 and 21-27 are rejected under 35 U.S.C. §103(a) as being unpatentable over the combination of Taira and Srivastava. The rejection acknowledges that Taira "does not teach the transcription terminator to be the neomycin resistant gene[,]" but instead that "Srivastava...teach[es] the use of antibiotic resistance genes in expression plasmids..., including neomycin resistant genes...[in] the selection of cells comprising such expression plasmids." Importantly, the rejection relies upon establishing *prima facie* obviousness, instead of an alternative rationale supporting the conclusion of obviousness.

The rejection fails to establish the third element of *prima facie* obviousness. This is because one of ordinary skill in the art would not have been motivated to combine the teachings of Taira and Srivastava to arrive at the subject matter of those rejected claims. First, Taira does not describe or suggest the insertion of a gene resistant to an antibiotic between the first lox site and second lox site

in an intervening DNA. In particular, paragraph [0124] in Taira states that:

> If required, it is also possible to allow a vector [which carries the expression system] to further carry a sequence that enables selecting cells transfected with the vector, such as a selection marker. Examples of selection markers include a drug resistance marker such as the neomycin resistance gene.

Thus, Taira teaches that the selection marker gene is to be inserted in the vector backbone, but not in an intervening DNA sequence flanked by lox sites and located between the sense and antisense sequences of an RNAi construct. Stated differently, Taira would have motivated one of ordinary skill in the art to insert a resistance gene in the vector backbone, not into a vector insert encoding a RNAi sequence. Applicants respectfully request that the rejection of Claims 17, 19, 21-25 and 27 be withdrawn.

In light of the foregoing, the Applicants respectfully request that the entire application is now in condition for allowance, which is respectfully requested.

Respectfully submitted,

T. Daniel Christenbury
Reg. No. 31,750
Attorney for Applicants

TDC:rb
(215) 656-3381